REMARKS

Entry of the amendments is respectfully requested. Claims 10, 15, and 16 have been amended. Claims 1-20 are pending in the application. Favorable reconsideration and allowance of this application is respectfully requested in light of the foregoing amendments and the remarks that follow.

1. Rejection Under §112, First Paragraph

Claim 10 stands rejected under 35 U.S.C. §112, ¶1. The Examiner contends that the previous amendment to claim 10 to recite a histocompability complex protein "other than HLA-DR" is new matter. To address this rejection, Claim 10 has been amended to remove "other than HLA-DR," as unnecessary to the claim. Applicant believes that Claim 10 as written is proper and fully enabled.

Claim 1 recites a formulation which comprises a ligand capable of binding to a HLA-DR protein, which is a class II histocompatibility complex protein (not class I as the Examiner stated in the Office Action). Claim 10 depends from Claim 1 and recites that the formulation further comprises an additional ligand to a protein, such as a histocompatibility complex protein. As such, a formulation of Claim 10 could include multiple ligands to histocompatibility complex proteins.

In light of the amendment to Claim 10, withdrawal of this rejection is requested.

2. Rejection Under §112, Second Paragraph

Claims 15 and 16 stand rejected under 35 U.S.C. §112, ¶2 as being indefinite. Claims 15 and 16 have been amended as suggested by the Examiner to recite that the HLA-DR protein is "acquired by" HIV. Accordingly, Claims 15 and 16 are definite, and withdrawal of this rejection is requested.

3. Rejection Based on the Prior Art

i. Rejections Based on Dufresne et al.

The Examiner has made various rejections based on Dufresne et al. These include the rejection of claims 1-9, 11-15, and 20 under 35 U.S.C. § 102(a) as being anticipated by Dufresne et al., the rejection of claims 1, 10, 12-14, and 17-18 under 35 U.S.C. § 103(a) as being unpatentable over Dufresne et al. in view of Zelphati et al, and the rejection of claim 1,12, and 19 under 35 U.S.C. § 103(a) as being unpatentable over Dufresne et al. in view of U.S. Patent Number 5,773,027 to Bergeron. The Applicant respectfully traverses all of the rejections based in whole or in part on the Dufresne et al. reference because the publication date of the Dufresne et al. reference is October 1999. The present application claims priority to Canadian application No. 2,270,600, which was filed August 3, 1999, and pre-dates the Dufresne reference. Accordingly, Dufresne et al. is not available as a reference under § 102(a). Accordingly, the withdrawal of the § 102(a) rejection based on Dufresne et al should be withdrawn.

In addition, the § 103 rejection based on the combination of Dufresne et al. and Zelphati et al. should also be withdrawn. The Zelphati et al. reference is discussed in the previous response. In the absence of the teachings of Dufresne et al., Zelphati et al. alone fails to teach or suggest Applicant's invention as claimed.

The rejection of Claims 1, 2, and 19 under § 103 is unpatentable over the combined teachings of Dufresne et al. and Bergeron should also be rejected. The Bergeron reference is discussed in the previous response. Bergeron alone fails to teach or suggest the invention as claimed.

Accordingly, the withdrawal of all rejections based in whole or in part on Dufresne et al is requested.

ii. Rejections Based Based on the Combined Teachings of Selvam et. al and Cantin et al.

Claims 1-2 and 10-18 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Selvam et al. (Antiviral Research 33:11-20 (1996)) in view of Cantin et al. (J. Virology 71(3):

1922-1930 (March 1997)). Claims 3-9 and 19 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Selvam et al. in view of Cantin et al. and further in view of U.S. Patent No. 5,773,027. Claims 1, 11, and 20 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Selvam et al. in view of Cantin et al. and further in view of Harlow et al. (in Antibodies, A Laboratory Manual, pp. 626-629 (1988)). These rejections are respectfully traversed for the following reasons.

First, combining Selvam et al. and Cantin et al. would change the principle of operation of Selvam et al. As such, the teachings of the references are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

Selvam et. al specifically teaches the use of anti-CD4 monoclonal antibodies conjugated to the surface of liposomes. (Abstract). Selvam et al. teaches that HIV predominantly attacks cells bearing CD4. (page 12, col. 1, second full paragraph). Selvam et al. uses anti-CD4 monoclonal antibodies to bind to CD4 on cells to deliver encapsulated phosphorothioate antisense complementary to the HIV *rev* region. (*Id.*). The Examiner recognizes that Selvam et al. fails to teach or suggest the use of a formulation with a ligand capable of binding to a HLA-DR protein, as recited in Claim 1 and the claims that depend therefrom. The Examiner cites Cantin et al. to cure this deficiency.

Cantin et al. teaches that HIV-1 and HIV-2 incorporate HLA-DR while budding out of infected cells and suggest that virally acquired host molecule is physically present on the surface of progeny virus. (page 1922, col. 1). In addition, Cantin et al. teaches that cellular activation leads to an increase in surface expression of HLA-DR glycoproteins. (page 1922, col. 2). The principle of operation of Selvam et al. involves targeting CD4, which is expressed on the surface of HIV infected cells. Modifying Selvam et al. based on Cantin et al's disclosure, as suggested by the Examiner, would result in targeting HLA-DR, which, unlike CD4, is expressed on both the surface of activated cells and the HIV virons themselves. This would change the principle of operation of Selvam et al., which employs liposomes with anti-CD4 antibodies that bind only to the surfaces of HIV infected cells.

The principle of operation of Selvam et al. would additionally be changed because CD4, to which the monoclonal antibody of Selvam et al. is directed, is expressed on both resting

T cells and activated T cells. (See pages 232 and 284 of Immuno Biology: The Immune System in Health and Disease, 4th ed., Janeway, C.T. et al.; attached hereto and incorporated herein by reference as Exhibit A). In contrast, HLA-DR is not; it is expressed only on activated T cells. (Cantin et al., page 1922, col. 2). Thus, if Selvam et al. were modified as suggested, the anti HLA-DR monoclonal antibody conjugated to the liposomes of Selvam et al. would target a molecule that is only expressed on activated T cells (as taught by Cantin et al.) instead of targeting both resting and activated T cells as taught by Selvam et al. This would further alter the principle of operation of Selvam et al. For at least these reasons, their teachings are not sufficient to render the claims *prima facie* obvious. *See In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

Secondly, an obviousness rejection cannot be supported merely by showing that it would be "obvious to try" the claimed invention. See, e.g., *In re Fine*, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless there is some objective teaching in the prior art suggests the desirability of the modification. *Id.*

Specifically, the Federal Circuit stated: "In some cases, what would have been 'obvious to try' would have been to ... try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave ... no direction as to which of many possible choices is likely to be successful...." *In re O'Farrell*, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

Cantin et al. lists numerous cellular components that are physically present on the HIV virion surface: HLA-DR, the HLA class I α chain, β_2 microglobulin, LFA-1, ICAM-1, CD43, CD55, CD59, CD63, and CD71. (Cantin et al., page 1922, col. 1). However, no direction is given in terms of which cellular component would be useful in a formulation which comprises a ligand capable of binding to a HLA-DR protein, as recited in Claim 1. Based on the unpredictability in the art, there would be no reasonable expectation of success that coupling an HLA-DR protein-binding ligand to a lipid-comprising vesicle would result in an effective formulation to bind HLA-DR. Accordingly, Applicant's formulation would not be obvious to one of skill in the art.

The Examiner has additionally cited U.S. Patent No. 5,773,027 against claims 3-9 and 19 and Harlow et al. against Claims 1, 11, and 20. However, neither of these references cures the base deficiencies in the teachings of Selvam et al. and Cantin et al.

The '027 patent teaches liposomes for the treatment of viral diseases and more particularly for the treatment of infections caused by viruses like human immunodeficiency virus (HIV) and cytomegalovirus (CMV). (Abstract). The '027 patent fails to provide any information about a ligand capable of binding to a HLA-DR protein, as recited in Claim 1.

Harlow et al. also fails to teach or suggest anything about a ligand capable of binding to a HLA-DR protein, as recited in Claim 1.

As such, neither of these references cures the base deficiencies in the teachings of Selvam et al. and Cantin et al.

Claim 1 is allowable over the prior art of record. Claims 2-20 depend directly or indirectly from Claim 1. Accordingly, withdrawal of the rejection of Claims 1-20 is requested.

CONCLUSION

Extension of Term. The proceedings herein are for a patent application, and the provisions of 37 CFR § 1.136 apply. Applicant believes that no extension of term is required. If any additional extension of term is required, please consider this a petition therefor, and charge the required fee to Deposit Account No. 23-2053.

It is submitted that the present claims are in condition for allowance, and notification to that effect is respectfully requested.

Respectfully submitted,

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